Biological Sciences Annual Report 1989/1990

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Organization: Division of Biological Sciences

Director General
I.C.P. Smith

Executive Assistant
A. Daley

Centre for Protein Structure and Design
P.R. Carey

Director, Laboratories
L. van den Berg

Director, Industrial Liason and Marketing
G.H.M. Adams

Management Committee

Medical Biosciences Laboratory
Head: G.M.H. Adams

Group	Group Leader
Molecular Physiology	R. Deslauriers
Cellular Oncology	J.F. Whitfield
Animal Resources	J.L. Bhasin

Carbohydrate Laboratory
Head: L. van den Berg

Group	Group Leader
Immunochemistry	D.R. Bundle
Anaerobic Bioprocessing	G.D. Sprott

Protein Laboratory
Head: P. R. Carey

Group	Group Leader
Protein Crystallogtaphy	D.R. Rose
Protein Biochemistry and Spectroscopy	G.E. Willick
Molecular Genetics	V.L. Seligy
Genetic Engineering of Proteins	S.A. Narang
Bioinformatics	M. Zuker

Administration and Services
Administrative Manager:
M. Dunlop

Service	In Charge
Office	C. Gobey
Electronic Design	—
Technical Services	J.P. Dumont
Supply	E.E. Grosser

Introduction

Scientific excellence combined with industrial and social relevance remain the driving forces for the Division of Biological Sciences. Our progress is indicated by the long list of scientific publications, the large and growing list of industrial collaborations and the extent of interactions with well-known research institutions, medical centres and industrial laboratories.

The Division is excited about its participation in two Networks of Centres of Excellence - Protein Engineering and Bacterial Diseases. The involvements reflect recognition by the scientific community of the expertise and the facilities resident in the Division. The scientific excellence of divisional staff was also recognized by the selection of Dr. G.D. Sprott for the 1989 Award of the Canadian Society of Microbiologists, and by Dr. M. Zuker as a Fellow with the Canadian Institute for Advanced Research.

A major collaborative project has been implemented with Allelix Biopharmaceuticals to develop analogues of human parathyroid hormone (PTH) for the treatment of bone disease. As part of our contribution to this project, the Division has achieved improvements in the expression of cloned PTH to levels of significant commercial interest. Development of generic technologies have yielded non-invasive NMR/MRI methods for the assessment of pathologic conditions in heart, liver, brain and pelvis. Other longer-term research projects have also shown exciting results. Antibodies elicited in response to and characterized by synthetic antigens have been cloned and sequenced, and the structures of two antibody binding sites have been resolved. Studies on the ether lipids of the new species *Methanosaeta concilii*, isolated in the Division, has led to the discovery of a novel hydroxydiether core lipid which appears diagnostic for the genus.

Ian C.P. Smith

The industrial and social impact of divisional efforts is also evident from the large number of industrial guest workers and graduate students working with our staff. Guest workers not only bring in new ideas and enthusiasm, they indicate the quality and relevance of the research being done, assist in the technology transfer, and take with them the advanced training that NRC can provide. Examples of the industrial collaborations with proven technology transfers include waste water treatment (Weston Research Centre, Paques Lavalin, Quesnel River Pulp), canola oil processing (CSP Foods), flavours (F&C International), bioherbicides and fertilizer enhancers (Philom Bios), bioreactor (Pegasus), vaccines and antibodies (IAF Biochem, Chembiomed) and gene technology (Labatts).

A major effort to bring the Sussex laboratories up to present day standards of safety and health is almost complete. At the same time, modest renovations are being done to provide a more effective working environment for our staff.

Further implementation of the recommendations from the comprehensive review process and the preparation of a more detailed Business Plan have led, and will continue to lead, to changes in programs to improve further the effectiveness and relevance of our research. The smooth implementation of changes that occurred this year is a tribute to the dedication and enthusiasm of our staff. It is in this spirit that they have achieved the high standards of scientific and technological development which are portrayed in this report.

Ian C.P. Smith
Director General

Industrial Liaison and Marketing Office

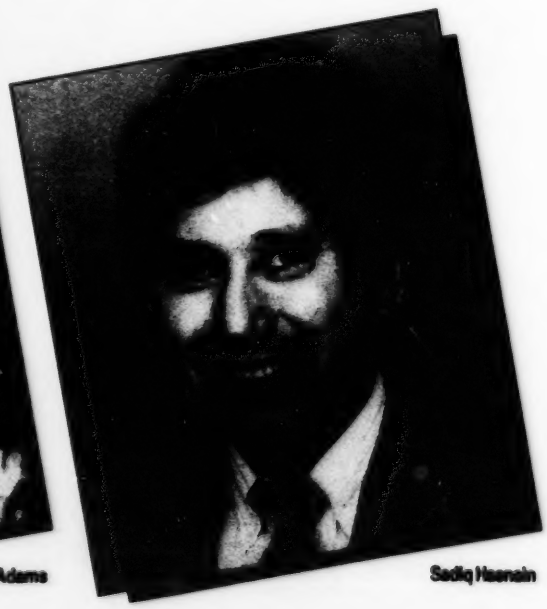
Director, Industrial Affairs:
G.H.M. Adams
Industrial Liaison Officers:
Protein Laboratory:
S. Hasnain
Medical Biosciences Laboratory:
J.P. Durkin
Carbohydrate Laboratory:
D.W. Armstrong
Marketing Services
Marketing Manager:
M. Brady

The Industrial Liaison and Marketing Office has two components. The Divisional component is headed by the Director, Industrial Affairs. Each laboratory has an Industrial Liaison Officer who time-shares these duties with laboratory research. The Marketing component is provided by a resident Marketing Manager from the Marketing Services Branch.

The Office facilitates and supervises technology transfer to industry. Results are presented in the highlights of industrial interactions in the Introduction and in the Table of Research Partnerships. These industrial interactions are increasing in number and extent and are becoming more effective as our clients are made aware of new technologies, services, and opportunities for research partnerships with the Division through a more consistent, systematic approach to marketing.

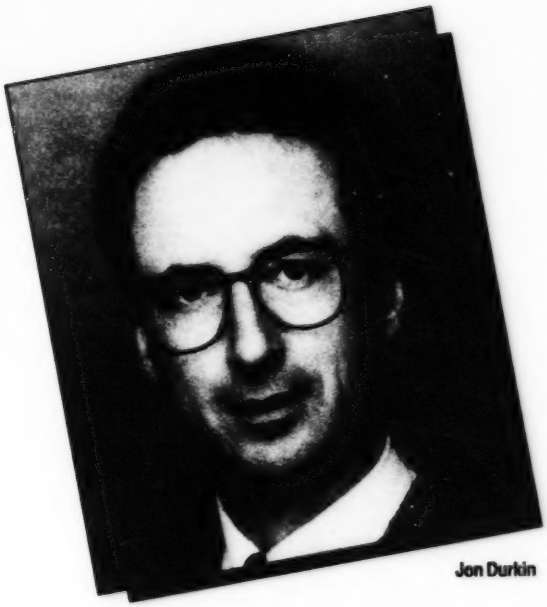
Three major thrusts were begun in 1989. One was the promotion of the expertise and the facilities of the Centre for Protein Structure and Design and the Protein Laboratory. The Allelix Biopharmaceuticals-Division of Biological Sciences joint project on parathyroid hormone (PTH) was a successful result of this effort. In collaboration with the Biotechnology Research Institute, a series of presentations and discussions were held with potential partners to assess interest in a consortium to do pre-competitive research in protein engineering. These discussions are continuing. The second major ongoing effort in the Industrial Liaison and Marketing Office is the assessment of the needs of the pharmaceutical and medical devices industries with respect to the application of Nuclear Magnetic Resonance Imaging and Spectroscopy in the testing of drugs and therapeutic devices. It is anticipated that effective programs will be put in place to serve the needs of these industries and the health care community. The third marketing activity involves the identification of potential clients for the Division of Biological

Gabrielle Adams

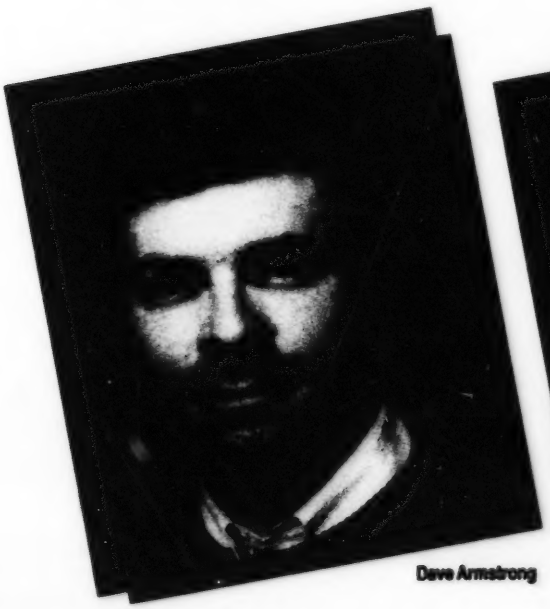

Sadiq Hasnain

Sciences expertise in anaerobic waste treatment with particular emphasis on pulp and paper wastes. Discussions are ongoing with two potential partners on developing advanced microbial waste treatment systems.

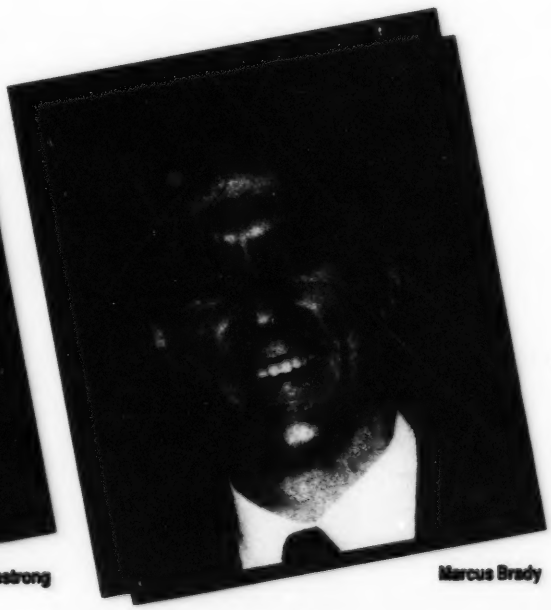
The activities of the Division were promoted at three Canadian conferences: Canbiocon '89, the Canadian Conference on Drug Safety, and the 5th NRC Industrial Biotechnology Conference. These general promotional efforts were in addition to many specific contacts with potential clients. The aim of these contacts, many of which are initiated informally by the Divisional scientists, is to develop joint research projects with industrial clients with financial and intellectual input from both parties and benefits to both industry and NRC.



Jon Durkin



Dave Armstrong



Marcus Brady

Centre for Protein Structure and Design

NRC's Centre for Protein Structure and Design provides and coordinates the high technology and expensive techniques which are needed to determine protein structure and properties. Thus, the expertise at the Centre consists of protein crystallography, protein nuclear magnetic resonance (NMR), powerful computational facilities and spectroscopic techniques such as circular dichroism (CD), fluorescence and Raman. The Centre is not a Protein Engineering Centre as such, but it does provide the essential biophysical support needed for protein engineering programmes. Of course, it can also characterize other novel (and interesting) proteins which are not part of protein engineering studies.

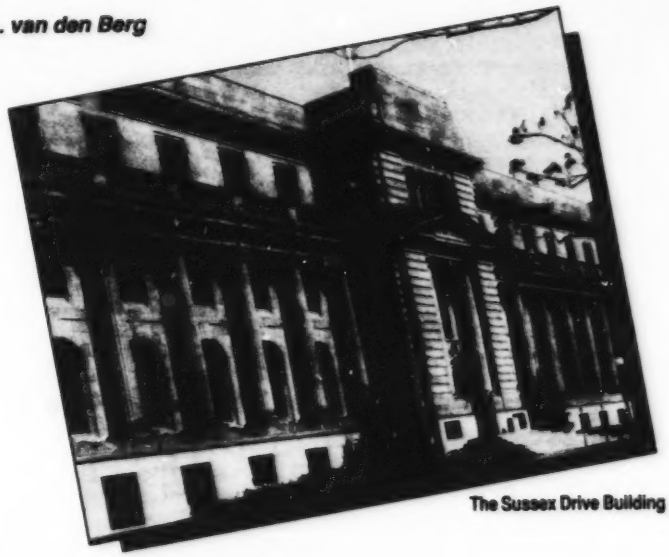
In order to provide the large investment in personnel and capital required by a state of the art Centre, resources have been allocated from both the Biotechnology Research Institute (BRI) in Montréal and the Division of Biological Sciences (DBS) in Ottawa. Thus, the instrumentation for 2-D protein NMR is located at the Biotechnology Research Institute. The Division's contribution to the Centre consists of its Protein Crystallography, Protein Biochemistry and Spectroscopy, and Bioinformatics Groups. In 1989, the Division set up a group to initiate solid state protein NMR studies. This builds on existing expertise at the Division of Biological Sciences and complements the work on proteins in solution undertaken at BRI. The groups associated with the Centre are housed in the extension to the Division's building at Montreal Road (M54), and have been provided with new equipment to provide up to date technology.

An important aspect of the Centre is that it provides a nucleation point for scientists from Canadian industry and universities to interact with NRC staff. Some of these interactions are simply of a service nature while others involve major collaborations on problems of mutual interest. In these collaborations, provision is made for industrial or academic scientists to stay at the Centre for long or short periods of time. To remain at the cutting edge of research, each group at the Centre spends a large fraction of its time engaged in fundamental studies, much of it in collaboration with academic and industrial scientists.

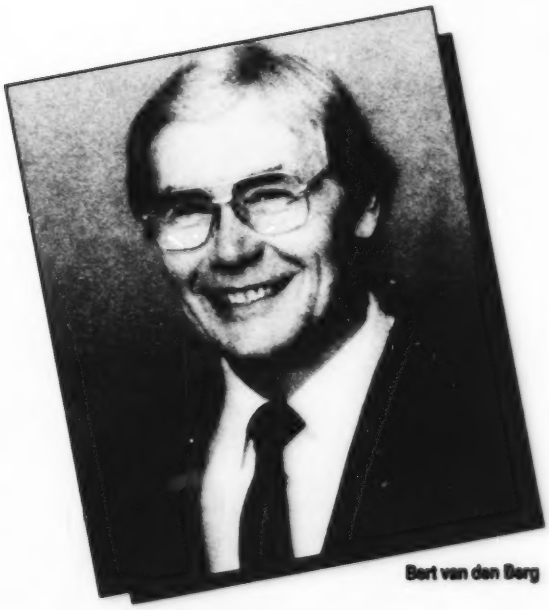
Industrial Guestworkers (Eric Zang, Nam Fong Han and Cathy Howlett) collaborating with Ivan Velliky and Karen Barber.

Carbohydrate Laboratory

Head: L. van den Berg



The Sussex Drive Building



Bert van den Berg

Immunochemistry
Group Leader: D.R. Bundle

Professional Staff:
E. Altman, J.-R. Brisson, D.R. Bundle, D.W. Griffith, H.J. Jennings, C.R. MacKenzie, M.B. Perry, J.C. Richards, N.M. Young
Research Associates:
A.N. Anderson, L.M. Beynon, K.P.R. Kartha, J. Kihlberg, M. Kulakowska, D. Leigh, B. Marsden, R. Oomen, A. Ragauskas, W. Severn, B.W. Sigurskjold
Technical Officers:
F.P. Cooper, R. Easy, E. Eichler, M.A.J. Gidney, R.A.Z. Johnston, R.A. Leitch, L. MacLean, S. Raymond, H. Seguin, B. Sinnott
Guest Scientists:
F.I. Auzanneau, B.M. Gudmundsson, K. Reimer, M. Wessels
Industrial Guest Scientists:
J.L. Di Fabio, B. Harrison, K. Holme, F. Michon, G. Muradia, R. Pon
Summer Students:
J. Larkin, J. Perry

Immunochemical problems that involve carbohydrate antigens at the molecular and cellular levels are the major interest of the Immunochemistry Group. Research focuses on primary and three-dimensional structure of bacterial and mammalian cell surface carbohydrates and their interaction with protein receptors such as antibodies and lectins. The aim is to understand in atomic detail the selectivity and exquisite differentiation of cell surface oligosaccharides by protein binding sites. This basic knowledge is regarded as a first step toward the modification and rational design of enzymes and carbohydrate receptors.

The diversified facilities of the group include a level E microbial containment facility, a monoclonal antibody production unit and an analytical laboratory providing facilities for high resolution nuclear magnetic resonance spectroscopy (Bruker AM200, AM500 and AM600 instruments) and combined gas chromatography - mass spectroscopy. An IRIS personal graphics workstation in tandem with microVAX 3500 and IBM mainframe computers are used for the modelling of carbohydrate antigens and antibodies.

The Group's physical resources and diverse expertise in areas of immunology, biochemistry, analytical chemistry and synthesis, combined with expertise available elsewhere in Canada and abroad, continue to be used to develop novel solutions to longstanding problems in clinical and veterinary microbiology. Emphasis is placed on the interpretation of biological activity in terms of the chemical properties and three-dimensional structures of the antigens and corresponding antibodies. This approach provides a scientific basis for the development of vaccines and diagnostics for human and veterinary diseases, and some of the results have been exploited by Canadian industries.

David Bundle and Roger MacKenzie going over an antibody purification problem.

HIGHLIGHTS OF PROGRESS

Conjugate Vaccine & Sialic Acid Research

The thrust of the research is a new generation of subunit vaccines using chemically defined parts of the native antigen that may be derived by chemical modification or synthesis. Particular targets are diseases caused by *Neisseria meningitidis* and group B *Streptococcus* organisms. Much of this

research involves industrial collaborations and applications.

The group specific polysaccharide antigen associated with group B streptococcal disease has been structurally defined and conjugated to tetanus toxoid. Antibodies to one of the epitopes of the group antigen shows promise for the possible development of a diagnostic kit against all group B streptococcal infections.

Molecular modelling studies with collaborators in France indicate that the group B meningococcal polysaccharide, an α2,8-linked homopolymer of sialic acid, can adopt a helical conformation. The unusual temperature dependency of the binding of poly A and the group B meningococcal polysaccharide to a human monoclonal antibody (IgM_{NOV}) is consistent with the conformational nature of the epitope.

Veterinary Diagnostics & Vaccines

The objectives of this program are the elucidation of the mechanisms involved in bacterial pathogenesis and the development of vaccines and diagnostics to combat important bacterial diseases of veterinary and related human interest.

An intensive study of the polysaccharide antigens of *Brucella abortus* and *Brucella melitensis*, the causal agents of brucellosis, has been successfully completed and the results are being exploited for the development of effective vaccines and diagnostic methods to combat the disease.

The work of the group has been particularly effective in characterizing and elucidating the structures of the capsules and LPS antigens of *Actinobacillus pleuropneumoniae*. This organism and *Pasteurella haemolytica* are two of the most important animal pathogens the group has investigated.

New investigations into the molecular and structural basis of bacterial pathogenesis are being undertaken as part of the NRC research contribution to the recently approved Network Centres of Excellence Program on Bacterial Diseases.

Molecular Recognition of Carbohydrate Antigens

The objectives of this research project which has become a focal point of the group's research is to understand at the molecular level how carbohydrate antigens and their protein receptors, antibodies and lectins, exert their biological function. Progress depends on the use of advanced technologies (nuclear magnetic resonance, molecular graphics, X-ray crystallography and genetic engineering), and a multi-disciplinary approach.

Antibodies elicited in response to and characterized by synthetic antigens have been cloned and sequenced. The Protein Crystallography Group has now solved the structure of two antibody binding sites and two antibody binding sites have also been constructed by a computer modelling approach. Mapping of the combining sites by synthetic analogs of the natural determinant has in three cases elucidated the hydroxyl residues that are hydrogen bonded to the binding site. The conclusions of these studies are that a small cluster of hydroxyl groups constitute the key polar contacts without which binding is abrogated. Complementary nonpolar interactions are also crucial to the integrity of association.

Jan Kihlberg and Eva Eichler in the carbohydrate synthesis laboratory.

The gene for a single chain antibody has been expressed in *E. coli* as part of a multidisciplinary antibody engineering project involving the Protein Crystallography and Genetic Engineering of Proteins Groups.

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Carbohydr. Res., 191: 295-303, 1989.

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Microb. Pathogen., 6: 455-458, 1989.

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In: Nucleic Acid and Monoclonal Antibody Probes: Applications in Diagnostic Microbiology. (Prakash, G. and Swaminathan, B., eds.). Marcel Dekker, New York, pp. 581-597, 1989.

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Biochem. Cell Biol., 67: 78-85, 1989.

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Biochem. Cell. Biol., 67: 278-280, 1989.

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Can. J. Chem., 67: 877-882, 1989.

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Capsular polysaccharides as vaccine candidates
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Contrib. Microbiol. Immunol., 10: 151-165, 1989.

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Fine structure of A and M antigens from *Brucella* biovars
Infect. Immun., 57: 2820-2828, 1989.

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Substrate specificity of naringinase, an α-L-rhamnosidase from *Penicillium decumbens*
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Am. J. Vet. Res., 50: 5-9, 1989.

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Block synthesis of two pentasaccharide determinants of the *Brucella* M antigen using thioglycoside methodologies
Can. J. Chem., 67: 497-502, 1989.

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Synthetic antigenic determinants of the *Brucella* A polysaccharide, a disaccharide thioglycoside for block synthesis of pentasaccharide and lower homologues of α-1,2-linked 4,6-dideoxy-4-formamido-α-D-mannose
Can. J. Chem., 67: 491-496, 1989.

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Structural analysis of the specific capsular polysaccharide of *Streptococcus pneumoniae* type 22F.
Can. J. Chem., 67: 1038-1050, 1989.

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Carbohydr. Res., 191: 53-62, 1989.

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Homology of the D-galactose-specific lectins from *Artocarpus integrifolia* and *Maclura pomifera* and the role of an unusual small polypeptide subunit.
Arch. Biochem. Biophys., 270: 596-603, 1989.

Fred Cooper with the GC Mass Spectrometer.

Anaerobic Bioprocessing
Group Leader: G.D. Sprott

Professional Staff:
E. Andras, D.W. Armstrong, S.J.B. Duff, K.G. Johnson, K.J. Kennedy, W. Khan, A. Kudo, R. Latta, W.D. Murray, R.P. Overend, G.B. Patel, H. Schneider, G.D. Sprott, I. Veliky, F.W. Welsh
Research Associates:
C. Choquet, N. Ross
Technical Officers:
B.J. Agnew, K.M. Barber, L.A. Brown, C.J. Dicaire, C.A. Elliott, L.P. Fleming, J.L. Labelle, K. Lamb, B. Methven, K.M. Shaw
Guest Scientists:
D.G. Grenzowski and H. Merks (Pegasus); S. Meakin and J. Nash (IDRC); R. Rutten and G. Wojtczak (F&C Int'l.); C.L. Light, N.F. Han, and P. Wang (Philom Bios Inc.); E. Zeng (Better Yield Insects)
Post Graduate Students:
P. McCarty (M.A.Sc.), A. Brown (Ph.D.)
Summer Students:
D. Agulnik, J. Bourgeois, A. Borque, C. Campbell, E. Francoeur, M. Hawara, R. Levitan, R. Little

Dennis Sprott discussing anerobic microbiology with Chris Choquet, a Research Associate.

Anaerobic waste treatment and development of novel products and processes are the main research areas of the group in studying the application of microbiology and enzymology. The major focus is on the development of new and improved anaerobic waste treatment systems to deal with difficult and toxic wastes and substances, and on the study and use of pure cultures of anaerobic bacteria involved in this treatment. A secondary focus is on the study and application of novel microbiological and enzymatic processes and products for the food industry.

The group represents an amalgamation of expertise that was present in three previous groups. The resultant multidisciplinary group is also responsible for the operation, use and maintenance of two facilities, the NRC culture collection, and the fermentation facility. The Group has strong collaborations with several industries, and many industrial collaborators work with the Group's staff members.

HIGHLIGHTS OF PROGRESS

Methanogenic Bacteria

Studies of metabolic pathways involving the labeling patterns in amino acids and sugars, following growth of various methanogens on ^{13}C precursors, showed that the degree of label randomization was low. These organisms can therefore be used for producing specifically ^{13}C or ^{14}C labeled compounds. Selection yielded a new isolate, a new species of *Methanobacterium*, which has an increased rate of production while maintaining the low degree of label randomization.

Studies on the major and minor ether lipids of *Methanosaeta concilii* (formerly called *Methanothrix concilii*) has led to a proposed scheme of interconversion during biosynthesis and the discovery of a novel hydroxydiether core lipid. Its unique structure appears diagnostic of the *Methanosaeta*.

As a continuation of the efforts on bioenergetics, the hydrogenase complex from *Methanospirillum hungatei* was purified and found to be about 750 kDa and hydrophobic. Its catalytic activity was enhanced by lipid extracts in keeping with membrane-hydrogenase interaction.

Recalcitrant Compounds

The major class of refractory compounds produced in the pulp and paper industries are lignin related aromatic fragments in varying degrees of reactivity and halogen substitution from the pulping and bleaching sections of the process. Degradation of representative model compounds such as syringic acid, catechols and chlorinated phenolics is being studied using enrichment and co-substrate systems. Certain compounds such as cinnamic, coumaric, and syringic acids are rapidly removed at a level of 2 g/L, while others are evidently more refractory. Polychlorinated aromatic phenols are anaerobically dechlorinated to mono- and di-substituted aromatic phenols.

Waste Treatment Processes

A new and increasingly used pulping technology, chemi-thermomechanical pulping (CTMP), produces a considerable quantity of extractives, including resin acids, in the wastewater. Anaerobic treatment of actual CTMP wastes has demonstrated that under starvation conditions these extractives are in fact toxic to the anaerobic microflora, while in co-substrate consumption tests they appear to be assimilated. Successful recommendations were made to Quesnel River Pulp, who have installed a full-scale anaerobic treatment system, on steps to be taken to minimize anaerobic sludge inhibition during a scheduled mill shutdown. Anaerobic treatment of its wastes provides the basis of an inter-divisional program with the Biotechnology Research Institute in Montreal. Work is also continuing on the improvement of the successful lagoon treatment of kraft pulp mill waste developed in collaboration with Diversified Research Labs.

Novel Processes

The overall objective is to develop processes, devices and instrumentation for the production of industrially desirable compounds, using whole cell or enzyme systems. Most of the emphasis has been on flavours and biopesticides as products.

Studies on refining of canola oil have led to the installation of a full scale process in Western Canada. Development of a cell culture bioreactor has reached the stage of testing of a commercial prototype to be produced shortly, while an IRAP project for development of technology for natural flavour production with F&C International, Inc., begun in January 1988, has reached the stage of scale-up to commercial production. Novel processes, which use lipases under low water content reaction conditions, have been developed for the production of flavour esters and emulsifiers.

Studies on fungal physiology and cultivation, and cell immobilization techniques have contributed to the development of commercial biopesticides, biofertilizers and a substantially less costly insect feeding system.

Studies directed toward understanding and control of catabolite inactivation in *Pichia pastoris* have now been completed. Alcohol oxidase is rendered susceptible to degradation by serine proteases through a protein kinase-mediated phosphorylation step. Process optimization in laboratory-scale reactor trials has resulted in the production of 130 g/l (3 M) acetaldehyde in 4 hours.

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Personnel of the
Supply Office (Stu Fletcher,
Peter Ashley, Terry Murphy, Ed Grosser, Joe Legari
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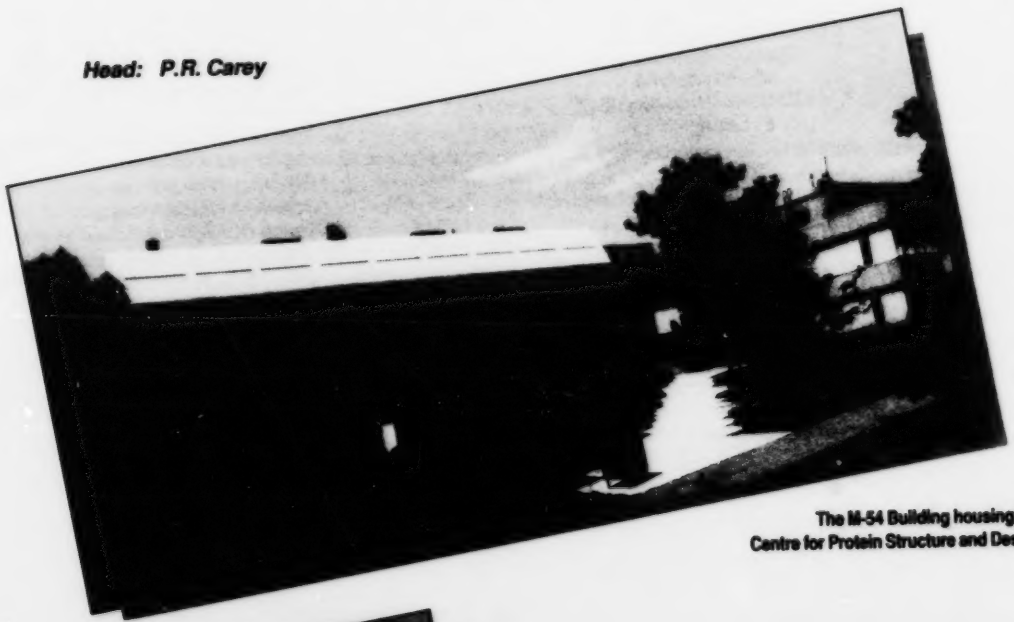
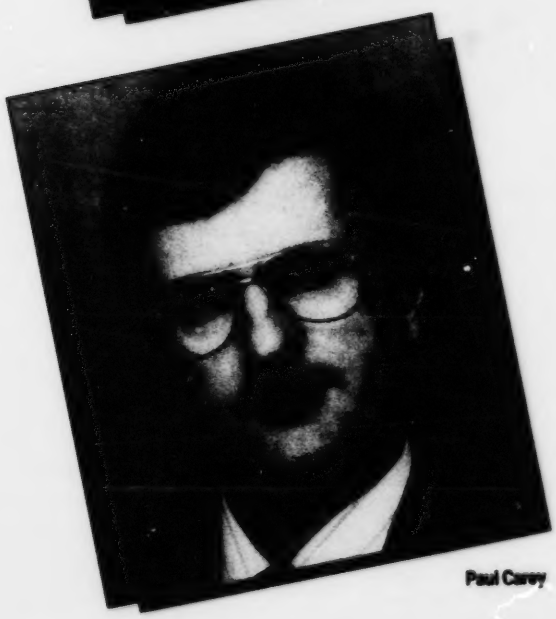
Protein Laboratory

Head: P.R. Carey



The M-54 Building housing the Centre for Protein Structure and Design



Paul Carey

Protein Crystallography
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Technical Officers:
M.E. Pippy, R. To
Guest Scientist:
M. Przybylska
Summer Student:
E. Leong

The primary objective of the group is to determine by crystallographic methods the three-dimensional structures of proteins, their mutants and complexes. This study is intended to enhance our understanding of the structure-function relationships and interaction of proteins, so that it may be possible to design and produce improved function-specific proteins or drugs. The main focus is on proteins which are under study by other groups in the Division or in Canadian industry.

Dave Rose, recently appointed Group Leader of the Protein Crystallography Group going over some results with Dr. Axel Brunger from Yale University.

As part of the Centre for Protein Structure and Design, the Group contributes expertise in protein crystallization, crystallo-graphic methodology, computing and molecular modelling. The laboratory contains state-of-the-art equipment for data collection, comprising a Rigaku high-power rotating anode Xray generator with graphite monochromator, a San Diego multiwire area detector system with two detectors, a Huber goniostat, and an online microVAX-3500 computer. Other major equipment includes a Nonius CAD-4 diffractometer and two interactive high-resolution computer graphics systems: an Evans & Sutherland PS-330 and a Silicon Graphics IRIS 4D/70 GT. Accessible computing resources include an IBM 3090 mainframe and a VAX 11/750.

The main thrusts this year have been in the following four areas: papain complexes and related cysteine proteases (collaboration with the Protein Biochemistry and Spectroscopy Group and groups at Biotechnology Research Institute); antigen binding antibody fragments (Immunochemistry Group); oncomodulin (Cellular Oncology Group); and xylanases (the Molecular Genetics Group, as well as Forintek Canada).

HIGHLIGHTS OF PROGRESS

Papain Complexes & Cysteine Proteases

Cathepsin B, which is a lysosomal cysteine proteinase with about 30% identity to papain, is implicated in some disease states such as muscular dystrophy and myocardial infarct. Good quality tetragonal single crystals have been grown for a sample from human liver, and monoclinic crystals were obtained for another sample from rat liver. Diffraction data have been measured to resolutions of 2.7Å and 2.4Å, respectively. For the tetragonal crystals, a very promising preliminary solution has been obtained by the molecular replacement technique, using the refined structure of papain as the search model.

The structures of two crystal forms of a papain-dodecamer complex have been solved, and show the dodecamer inhibitors in broadly similar conformations in the two structures. The detailed enzyme-inhibitor interactions, however, appear to differ significantly.

Antigen Binding Antibody Fragments (Fab's)

Crystal structures of Fab's from two bacterial polysaccharide antigen families are being studied as part of a multidisciplinary divisional effort to understand the details of molecular recognition of carbohydrate antigens by proteins. The structure of an unliganded Fab specific to *Brucella abortus* has been determined and is being refined with 2.5Å data. Its complex with an oligosaccharide has been crystallized and its crystal structure is being determined. A parallel study, on which we are collaborating, has produced the crystal structure of a Fab specific to *Salmonella* as a complex with the tetrasaccharide hapten, and as a complex with the dodecamer of three hapten-repeating units.

Oncomodulin

The crystal structure of oncomodulin, a tumour-related calcium-binding protein, has been refined with 1.85Å data. Beside the two intramolecular calcium ions expected, the crystal structure has been found to contain an intermolecular calcium, which together with its symmetrically related equivalents link the oncomodulin molecules into continuous sheets. Such an arrangement has not been observed in other structures of the troponin C family of calcium-binding regulatory proteins. The surface side chains of oncomodulin, Gln 54 and Gln 71, appear to be conducive to this molecular aggregation.

Xylanases

Genetic and industrial interests in xylan-degrading enzymes, especially the xylanases that exhibit no cellulolytic activity, have led us to study the structure of a xylanase from *Bacillus circulans* cloned into *E. coli*. Highlights of work on these crystals include the identification of three potential heavy-atom derivatives. High quality area-detector data from native and derivative crystals are being analyzed.

Farid Ahmed, former Head of the Protein Crystallography Group.

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Protein Biochemistry and Spectroscopy
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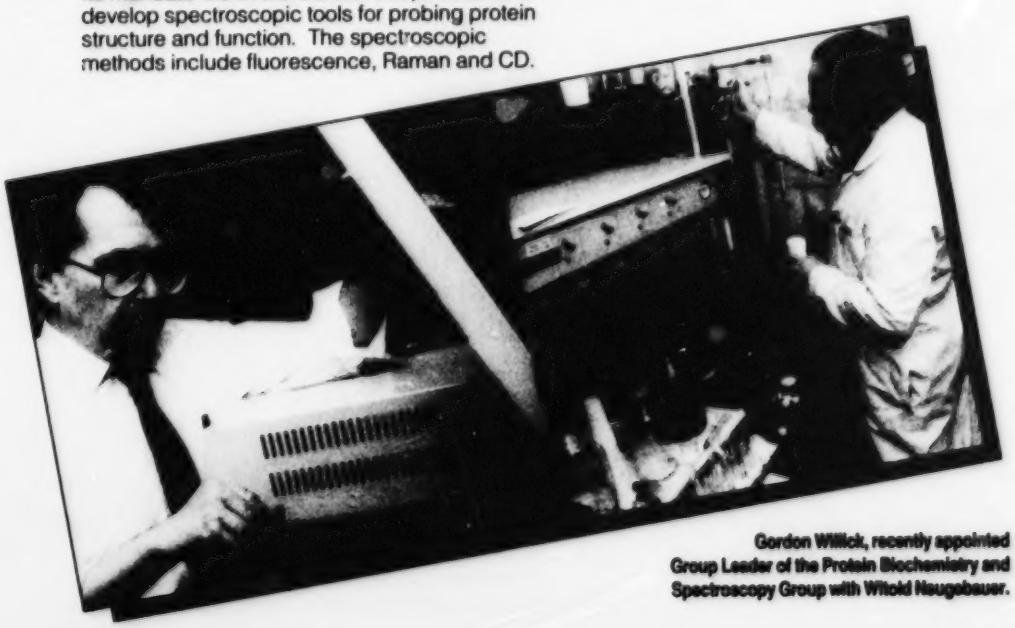
Summer Students:
B. McDonald, S. van der Waart, N. Methot

This group forms part of NRC's Centre for Protein Structure and Design referred to earlier. Its mandate within the Centre is to provide and develop spectroscopic tools for probing protein structure and function. The spectroscopic methods include fluorescence, Raman and CD. At the end of 1989, the repertoire was extended to include solid state NMR spectroscopy. Although each method offers insights into one or more aspects of proteins, the work at the Centre concentrates on focussing all possible techniques to define the properties and mode of action of a "targeted" protein.

The section has major involvement in three large projects which span other NRC Divisions and industrial collaborations. These are the cysteine proteases, with emphasis on cathepsin B; parathyroid hormone; and the insecticidal protein from *Bacillus thuringiensis*. Each of these projects involves group members in significant protein purification and characterization at the biochemical level before physical characterization is attempted.

To stay at the forefront of protein spectroscopy, some developmental work is undertaken. The facilities include steady state and time resolved fluorescence instrumentation, with the latter being based on a laser pumped dye-laser; scanning and multichannel Raman spectrometers with a range of visible, near UV and UV excitation sources; a Jasco J-600 CD instrument; and a Varian Unity wide bore 400 MHz solid state NMR spectrometer.



Gordon Willick, recently appointed Group Leader of the Protein Biochemistry and Spectroscopy Group with Witold Neugebauer.

HIGHLIGHTS OF PROGRESS

Fluorescence Laboratory

The value of progress in instrumentation is best demonstrated by recent work on hemoglobin and myoglobin. Contrary to reports in the literature, it was shown that the structural relationship of the A helix to the rest of the protein is not affected on changing the nature of the heme ligand in both proteins.

In collaboration with the Cellular Oncology Group and Biotechnology Research Institute, several specific site directed mutants of oncomodulin were studied for their use in time resolved fluorescence immunoassays. Based on an assessment of the role of each of the two calcium ions which bind to oncomodulin on the protein structure, peptide/protein lanthanide chelators were developed. The first phase showed that sensitivities equivalent to or better than other fluorescence based systems were obtained.

Raman Laboratory

A number of experimental innovations led to very high quality resonance Raman data of enzyme substrate complexes "on the fly". It was possible to observe the effects on an active site carbonyl group of "switching on" the enzyme's catalytic apparatus by changing pH. For a series of substrates, the kinetic parameters could be related to a change in the properties of the carbonyl group.

Protein dynamics are being probed by obtaining resonance Raman spectra of enzyme bound substrates at very low temperatures - down to 4K. The data provide insight into the number of conformational sub-states of proteins and in the way the enzyme uses energy to drive a chemical reaction.

Parathyroid Hormones

Parathyroid hormone (PTH) is an 84 amino acid hormone with potential in therapies for conditions such as osteoporosis. The project involves close and extensive collaborations with Allelix Biopharmaceuticals and a number of other groups at NRC. The objectives of the programme are to produce enough PTH for biological and biophysical characterization, and for clinical trials. Characterization of PTH is aimed at designing novel and more effective analogues. PTH has been purified from yeast and *E. coli* expression systems. The PTH gene was synthesized and cloned into these cells in the Molecular Genetics Group. From the yeast expression system, several fragments from the NH_2-terminus and COOH-terminus were identified. Expression of PTH in *E. coli* has produced 10-30 mg/L, and the expressed products are almost entirely intact PTH. A set of deletion fragments of PTH^{1-34} have been purified which are currently being tested for biological agonist or antagonist properties in the Cellular Oncology Group.

Cathepsin B

Protein engineering of the key human cysteine protease, cathepsin B, is being carried out in collaboration with Dr. J. Mort of the Shriner's Hospital in Montréal. Our efforts have focussed on the purification and crystallization of human liver cathepsin B and a recombinant rat cathepsin B expressed in yeast. The solution of the structures by the Protein Crystallography Group is well underway and will lead to the design of inhibitors with potential therapeutic value.

Bacillus thuringiensis

The group's involvement with *Bacillus thuringiensis (Bt)* which produces environmentally acceptable protein pesticides, has been part of a network involving three Divisions of NRC, Forestry Canada, and the Universities of Ottawa and Sudbury. The group's role has been in the area of purification and characterization of the *Bt* proteins. Extensive investigations to reduce the sunlight-induced instability of *Bt* proteins have been completed and much of this technology has been transferred successfully to industry. In the past year HPLC methods have been used to purify and characterize the closely related proteins produced by individual *Bt* strains.

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Molecular Genetics
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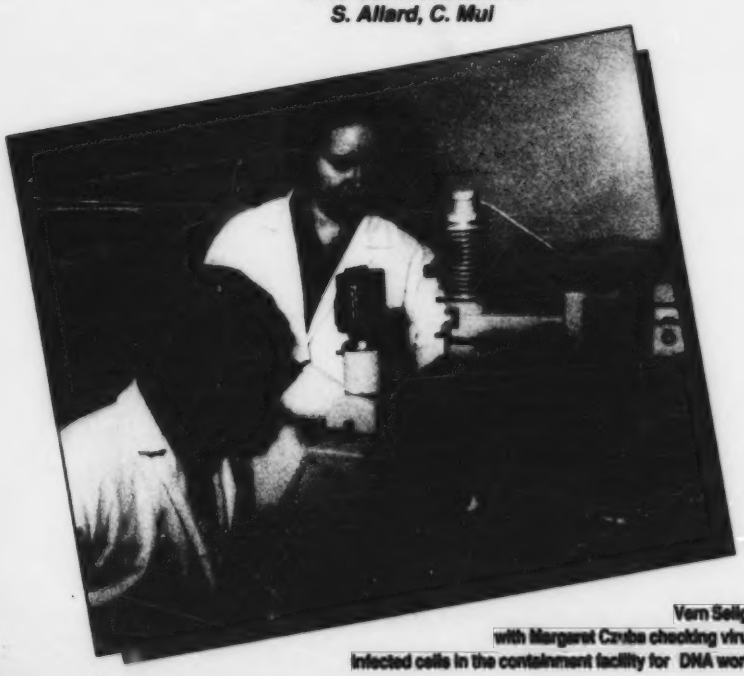

Vern Seligy with Margaret Czuba checking virus infected cells in the containment facility for DNA work.

The Molecular Genetics group combines its expertise in cell biochemistry, genetics and molecular biology to study proteins of fundamental and applied importance which are of interest to collaborators in other NRC groups and laboratories in government, industry and university. Molecular genetics permits the identification, molecular characterization and functional analysis, by mutation, of any protein regardless of its biological origin.

The group's research is focussed on three generic areas which deal with the characterization and production of (i) enzymes; (ii) regulatory proteins that affect cell growth and differentiation; and (iii) genetically engineered organisms. Protein sequencing is an essential part of this research and is available as a service to outside interest groups.

Present research efforts, including updating of facilities, are shifting to the development of technical resources in the areas of "protein engineering" and "molecular cytogenetics" for use in the scale-up production of animal proteins, in the elucidation of transcriptional events during cell differentiation and in genomic mapping studies.

HIGHLIGHTS OF PROGRESS

Characterization and Production of Enzymes

Links with industry and with the MRC/NSERC Network Centres of Excellence for Protein Engineering have contributed significantly to this subproject's focus which deals with structure-function studies of glycosidases and proteases of commercial and medical interest. Computer analysis of twenty different glycosidase genes has recently led to the design of four important mutants which identified three essential amino acids involved in enzymatic function of two highly divergent endoglucanases. From this same mutation work, an expression vector for secretion of heterologous proteins has been made and is now being used by other institutions for their research.

Native and mutant *Bacillus* xylanases and two fungal xylanases have been characterized for use in X-ray crystallographic studies. Work with the Labatts Research Centre has led to the molecular characterization of a co-regulated, fatty acid degrading enzyme and its gene and pseudo gene component. These genetic elements are useful in other applications, including analysis of mammalian enzyme function. The complete amino acid sequence of two proteases has also been obtained, enabling function studies to begin.

Regulatory/Structural Proteins

In both higher and lower organisms, most proteins that modulate expression of genes during switches in cell metabolism and cell/tissue development (e.g. receptors, trans-acting inducers and repressors, hormones and growth factors) have not been characterized so far. The long-term goal of this group is to produce natural or synthetic analogues of such proteins in native or heterologous hosts for the elucidation of their molecular structures and functions and their application in health care and biopharmaceutical sectors.

Recently, synthetic genes coding for human-like proinsulin and parathyroid hormone (PTH) have been redesigned and found to produce intact product in high yield using a bacterial host. A new assay for analysis of PTH has been introduced and purification and amino acid sequences of PTH have been carried out. Large scale production and physical characterization of PTH are the key objectives for the NRC-Allelix Biopharmaceuticals strategic alliance which has been recently organized. Testing of PTH-related hypercalcemic factor is being done by an outside group.

Significant advances have been made in defining the molecular events involving host-cell gene involvement in the expression of a broad host range, cytoplasmically replicating insect *Iridovirus*. Small-scale cell culture systems have been established for parallel studies of expression and function of iridovirus and mammalian genes. A semipermissive cell line, a plaque assay for detection of cloned virus as well as cytological and fluorescent probes, have been developed to study changes in cellular architecture during production of nuclear matrix-like, viroplasmic centres. Characterization of a polyprotein similar to that of mammalian leukemia viruses is now complete and the identification of factors regulating the expression of this gene, the genes for the major coat protein (Capsid) and a human neurafilament-like polypeptide, are in progress with the objective to develop novel expression systems for production of animal proteins.

Genetic Engineering of Organisms

A bench-scale fermentation system has been established and used to furnish details on the production and purification of target proteins from engineered plasmids carrying PTH and glycosidases. A novel, putative cell growth regulator is also being tested using an engineered gene whose product normally blocks replication of nucleated red blood cells. Expressions of this gene and a related iridovirus gene have been put under control of a carbon catabolite regulated promoter.

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Arch. Biochem. Biophys., 270: 596-603, 1989.

Mike Dove
using the 2-D densitometer.

Genetic Engineering of Proteins
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The main goal of this group is to design and produce novel proteins of potential medical and industrial importance by synthetic genes and by using the recombinant DNA approach. Our research efforts are focussed on antibody fragments.

Monoclonal antibodies have been produced by hybridoma technology, but their use for diagnosis and treatment of human diseases is still limited. Broader application requires larger scale production, higher specificity and lower immunogenicity, all possible by the application of recombinant DNA and synthetic gene technology as developed in this laboratory.

Joe Michniewicz and Saran Narang studying a DNA sequence.

The group's efforts are directed towards making antibodies more human compatible, by making them smaller in size while maintaining or improving specificity. This in turn lowers the immunogenicity of these proteins in man, while optimizing their binding affinity, pH profile, bispecific conjugate to drugs, isotopes or toxins. Potentially these modified monoclonal antibodies will be useful in the treatment against cancers, and heart and other diseases.

HIGHLIGHTS OF PROGRESS

A 1450-base pair DNA sequence encoding the monoclonal antibody fragment specified for the *Salmonella* serotype B 0-antigen was designed using the *E. coli* preferred codons. It was chemically synthesized by ligation of synthetic fragments into a linearized plasmid followed by transformation. Using this technique, light chain γ_1 has been expressed successfully in *E. coli*. After isolation and purification of this synthetic fragment, heterologous recombination with mouse heavy chain gave an active antigen-binding protein in 15-20% yield. Inhibition experiments with the polysaccharide antigen in comparison with the natural antibody indicated comparable binding rates for the natural and synthetic antibodies.

The DNA encoding for the light chain of the antibody (V_L) has been linked to the DNA of the heavy chain (V_H). On expression in *E. coli*, a protein of the expected molecular weight has been found to be retained on the affinity column made of 0-antigen. This observation suggests the single chain antibody is active. Also, a universal hinged region has been designed and linked at the end of V_L and V_H genes and expressed in *E. coli*.

Purification of antibody fragments from *E. coli* is a major problem. This problem has been overcome by incorporating a small peptide signal in the plasmid. This peptide has a special affinity property which can be used in the purification of any protein expressed in *E. coli*.

There are six amino acid differences between the V_L of Brucella and blood group A. Their simultaneous synthesis has been achieved by cloning mismatched DNA. This is a novel approach to diversify antibody genes synthetically.

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Applied and Environmental Microbiology. 55: 1192-1195. 1989.

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This Group uses mathematical and computer science tools to study the growing database resulting from the rapid DNA sequencing technology and international projects to map sequence entire genomes. These databases comprise genetic sequence, protein structure and other molecular biology data. Applications are to the understanding of gene regulation and protein folding, as well as to managing and interpreting the information flowing from the Human Genome Project. This new field (see von Heijne: Sequence Analysis in Molecular Biology, Treasure Trove or Trivial Pursuit) has been legitimatized in 1989 by the creation of the National Center for Biotechnology Information by the U.S. Congress.

In January 1989, Dr. Zuker began a five-year appointment as a fellow of the Canadian Institute for Advanced Research (CIAR). This links the Bioinformatics Group with the CIAR's Evolutionary Biology program, which is a network of biologists, biochemists and mathematicians from all over Canada. The CIAR connection has led to links with genome mapping and sequencing projects: the Center for Prokaryotic Genome Analysis at the University of Illinois and a proposed organelle sequencing facility at the University of Montreal.

Because of the essential role of computers in the field, the Group plays a central role in computing within the Division. The group operates a VAX minicomputer for general use in the Protein Laboratory, and a smaller minicomputer devoted to molecular genetics computing. It is responsible for overall computer related planning and for networking. Staff are also consultants to the Molecular Biology Database Service run by the Canada Institute for Scientific and Technical Information (CISTI). The group is converting from VAX, PC's and the IBM mainframe to powerful and efficient UNIX workstations linked to a large and compatible UNIX server that will serve the entire Division. In addition, the recent arrival of the Internet to NRC allows easy access to remote computers world-wide.

The Group currently works on biomolecular structure prediction, molecular sequence alignment algorithms, and methods to assign a structure or function class to a protein starting from the primary sequence information.

Mike Zuker and Roland Gaboury at a computer workstation.

HIGHLIGHTS OF PROGRESS

Biomolecular Structure Predictions

The modelling of RNA structure is accomplished by free energy minimization using a discrete optimization algorithm that deals only with the secondary structure. This is appropriate, because phylogenetic data from comparative sequence analysis, as well as data from chemical modification and enzyme cleavage experiments do not give three-dimensional structure information. An active collaboration is maintained with a biochemistry group that provides the experimental data for base stacking energies and loop destabilizing energies.

A novel mathematical technique to determine close to optimal solutions of dynamic programming problems has led to a powerful and effective algorithm and computer program for predicting families of RNA foldings close to the computed minimum free energy. This program has already attracted much interest internationally, and two computer companies are converting the code to run on their supercomputers. It has been used recently in the group to predict common folding patterns in the 5' untranslated regions of a group of small RNA viruses.

In contrast, protein structure modelling uses energy minimization of a three-dimensional continuous model in which residues are approximated by single points, or in which each non-hydrogen atom is modelled separately. Empirical pairwise potentials are used. This more detailed modelling is appropriate because of a database of protein structure models deduced from X-ray diffraction and NMR data.

A new way to minimize differentiable functions of many variables that can overcome the multiple minimum problem is being applied by the Group to computing global energy minima for models of small polypeptides that approximate residues by single points. One recent practical advance in protein structure modelling stores the coordinates of a protein chain in a binary tree form, allowing for a rapid and efficient determination of the nearest neighbours of each residue.

Molecular Sequence/Structure Alignment

The same idea that made the suboptimal RNA folding algorithm possible has been applied to an automatic and objective algorithm for aligning protein structures in three dimensions. This enables not only the optimal alignment of protein structures, but also an assessment of how well defined the various parts of the alignment are. The three-dimensional alignment algorithm has been speeded up by an order of magnitude, and the associated three-dimensional motif searching program has also been improved and extended. It has been used in the past year to select candidates from the database of protein structures for modelling hypervariable regions of immunoglobulins.

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The Electronic Design and Technical staff (André Simard, Randy Holmes and Bob Toews) (Verner Kasperek, Rudi Mausser and Don Harris).

Medical Biosciences Laboratory

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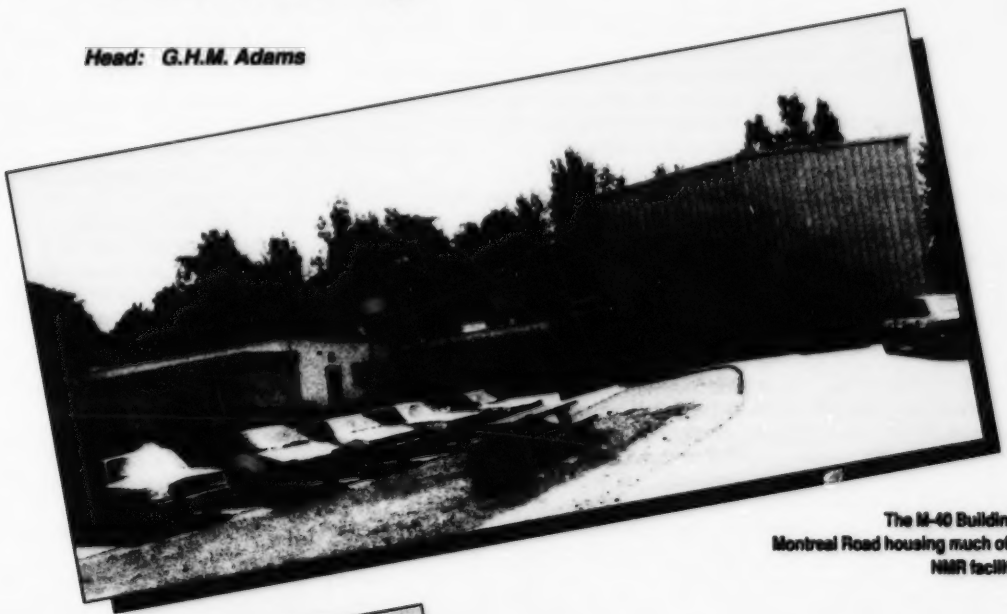

The M-40 Building at Montreal Road housing much of the NMR facilities.

Gabrielle Adams

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Roxanne Deslauriers and Kieran Clark at work at Building M-40.

The Molecular Physiology Group investigates biomedical problems with particular emphasis on Nuclear Magnetic Resonance (NMR) Spectroscopy and Imaging. The group develops and adapts NMR techniques for biomedical research and diagnosis using a Biospec 4.7/30, AM-360, MSL-300, as well as a home-built 200 MHz NMR spectrometer. Applications focus on heart disease, stroke, cancer, liver and membrane function. Facilities for animal housing, surgery, and physiological and biochemical measurements are also available within the group.

The goal of the group is to study physiology and pathology non-invasively. This allows metabolism to be measured repeatedly in the same subject leading to better understanding of disease processes and improved diagnosis.

The group has a wide client base in universities, hospitals and industry as a direct consequence of the expertise developed in basic research within the Molecular Physiology Group. Collaborative research with clients is supported by research grants from government, private charitable funding agencies and by contracts from industry. The Molecular Physiology group is closely involved with universities for graduate level training in biomedical magnetic resonance spectroscopy and imaging.

HIGHLIGHTS OF PROGRESS

Non-Invasive NMR Techniques for Living Systems

To improve and develop non-invasive NMR techniques, probes for both imaging and spectroscopy have been built to increase the time resolution of measurements of neuronal damage in the rat model of stroke. Shielded gradient coils with eddy current settling time of the order of one millisecond have been designed, built and tested. These allow experiments using multi-slice, multi-echo imaging sequences with an inter-echo time reduced to 22 milliseconds. Problems have been experienced in quantitating metabolites in perfused organs when tissue swelling has changed the sensitivity of the probe. A novel 4-coil probe has been designed and built in collaboration with the National Institute of Health (USA) to overcome this problem. A microprobe that simultaneously measures NMR

spectra and contractility of human atrial trabeculae has been designed, built and successfully tested.

Software developments include implementation of adiabatic pulses on spectrometers at NRC and at the Ottawa General Hospital to increase the usefulness of surface coils and to improve spatial localization techniques for *in vivo* spectroscopy. The chemical shift imaging (CSI) technique is in use on the spectrometer at the Ottawa General Hospital.

Applications of NMR Spectroscopy and Imaging to Physiological, Medical and Pharmaceutical Problems

NMR studies of heart preservation showed that, with high concentrations of buffer, the high energy phosphate compounds in human atrial appendages (removed during bypass surgery) were better preserved up to 6 hours at 12°C than at 4°C. Porcine hearts showed less damage after 12 hours of ischemic preservation at 5°C than at 12°C. A porcine model of acute left coronary insufficiency has been developed and phosphokinase C activation in ischemic reperfused ventricular muscle has been demonstrated.

Microimaging and spectroscopy performed on a forebrain ischemia model of stroke demonstrated good correlation between magnetic resonance imaging data and histochemical data. Neuronal injury is both spatially and temporally dependent, and magnetic resonance images appear normal four days following stroke. The effects of caffeine, alcohol and pharmaceutical agents on the rat following a stroke have been evaluated. Both acute, and regionally selective, delayed openings of the blood-brain barrier were identified as important in a rat model of forebrain ischemia shown to evoke brain edema. Entry of blood-borne domoic acid (the mussel toxin found in Eastern Canada) into different brain structures was characterized as it relates to associated neurological damage and amnesia.

NMR spectroscopic studies of chronic alcohol liver disease in rats have demonstrated decreased levels of high energy phosphates which correlate in severity with histopathological changes. Oxygen consumption and blood flow measurements demonstrated the possibility of making physiologically meaningful measurements by NMR on intact conscious animals.

Quantitation of the rate and nature of motions occurring in lipids and membranes have been achieved using relaxation, lineshape and 2-D NMR analyses of deuterium and phosphorus spectra.

1-D and 2-D ^{1}H-NMR data from biopsies of human cancers have shown good correlation with histophathology suggesting the possibility of using NMR for cancer diagnosis *in vivo*.

The *in vivo* distribution permeation and excretion of a common contrast reagent used to quantitate sodium distribution in tissues has been determined. The NMR visibility of sodium, using quantitative NMR methods and flame photometry in the presence and absence of shift reagents, has been shown to be over 80%.

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Cellular Oncology
Group Leader: J.F. Whitfield

Professional Staff:
J.P. Durkin, J.P. MacManus, R.H. Rixon, J.L. Schwartz, M. SikorskaWalker, P.R. Walker, J.F. Whitfield
Research Associate:
J. KwastWelfeld
Technical Officers:
R. Ball, L. Dvarionas, R.J. Isaacs, J.M. LeBlanc, G.A.R. Mealing, R.G. Tremblay, T. Youdale
Guest Scientists:
E.K. Asem, J. Filipski, S. Jacobson, V. Krsmanovic
NSERC Fellow:
B.R. Chakravarthy
Graduate Students:
I. deBelle, L. Fournier
Summer Students:
T. Binder, S. Walsh

The continuing overall goal of the Cellular Oncology Group is to determine how normal animal cells switch from a non-proliferative to a proliferative mode and *vice versa* and what goes wrong with these switching mechanisms to produce cancer. During the last twenty years the group has identified Ca^{2+}-binding proteins, Ca^{2+}-dependent "signalling" protein kinases, cyclic AMP and cyclic AMP-dependent protein kinases as principal participants in the events leading to the onset of chromosome replication. The evidence indicates that the disturbance of or the loss of the need for membrane-based Ca^{2+}-dependent signalling mechanisms is at least a major part of the dysregulation and ultimate deregulation leading to cancer cell proliferation.

Jim Whitfield of the Cellular Oncology Group.

Currently, there are four areas of study in the group's research: gene expression and DNA replication, antidifferentiation factors, signal transduction, and characterization of the cancer-specific protein, Oncomodulin.

HIGHLIGHTS OF PROGRESS

Gene Expression and DNA Replication

Investigations into the deregulation of cell proliferation includes determining the changes in chromatin structure, gene expression and enzyme activities that are responsible for proliferative activation and the subsequent initiation of DNA replication and mitosis. Since the rat liver is still the only experimental model in which a very large accessible mass of non-proliferating, unquestionably normal cells can be stimulated to switch synchronously and temporarily into a proliferative mode, considerable effort is committed to finding out how these cells use Ca^{2+} and cyclic AMP signals to control the production, assembly, and activity of the subunits of one of the principal DNA replication enzymes, ribonucleotide reductase. Two ways in which cells control ribonucleotide reductase were discovered. These are ubiquitination and glycosylation of one of the subunits (M1). Ubiquitination sensitizes the nascent M1 subunits to proteolytic degradation. However, when cells start proliferating they stop ubiquitinating the M1 subunits, and instead glycosylate and combine them with M2 subunits to make active holoenzyme which is inserted into the outer nuclear membrane to provide the deoxyribonucleotides for DNA synthesis. Also, during the last year, much progress has been made in isolating and characterizing chromatin loops with a view to ultimately defining the structural changes that underly the sequential coordinate expression of specific blocs of genes during the cell cycle, differentiation and carcinogenesis.

Antidifferentiation Factors

A major Franco-Canadian joint venture involves the characterization and exploitation of two newly discovered hemopoietic antidifferentiation factors which specifically block the differentiation of avian, human, and murine erythroid precursor cells. If such factors are produced by leukemia cells, they will enhance leukemogenesis by locking the producer cells into an active proliferative state and preventing them from responding to differentiation factors.

Signal Transduction

Signals that switch on proliferation are being revealed by measuring Ca^{2+} channel activity, and exploiting new methods for measuring internal Ca^{2+} levels and membrane-associated protein kinase C activity. In particular, these techniques are being used to find out how various hormones, growth factors and two viral oncogene products (the avian sarcoma virus' pp $60^{v\text{-}src}$ tyr protein kinase, and the Kirsten sarcoma virus' p21 RAS protein) signal quiescent cells to start proliferating. A highlight of the year's research has been the demonstration that a key part of the primary mitogenic signals induced by the two viral oncogene products is a transient Ca^{2+}-dependent surge of membrane-associated protein kinase C activity.

The new protein kinase C method recently developed in this group has revolutionized the understanding of how parathyroid hormone signals cells. It is now clear that this hormone stimulates adenylate cyclase and membrane protein kinase C via independent pathways. The realization that there are two different signal pathways greatly improves the ability to bioassay and functionally characterize the recombinant parathyroid hormone and its derivatives that are being produced in the Division for possible industrial exploitation as biopharmaceuticals.

Oncomodulin

Some years ago exploration of the universally disturbed role of Ca^{2+} in the control of cancer cell proliferation led to the discovery of a new Ca^{2+}-binding protein, Oncomodulin. This protein appears in 94% of all adult human or rodent cancers but never in normal adult tissue. It was found that the only "normal" cells that produce oncomodulin are the highly invasive, destructive, quasi-metastatic cells of the embryonic cytotrophoblast, but not the moving, shaping, proliferating cells of the embryo itself. This suggests that oncomodulin is part of, or a byproduct of, an invading/spreading mechanism that is specifically designed to serve some function in the early embryo's probing, pioneering, placenta-forming cytotrophoblast cells. Its role in the cytotrophoblast may reveal its role in adult cancer cells.

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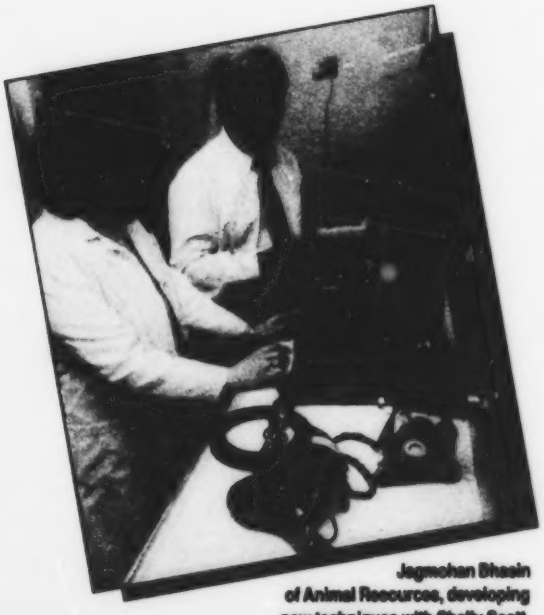
Animal Resources
Group Leader: J.L. Bhasin

Professional Staff:
J.L. Bhasin
Animal Care Staff:
J. Daoust, M. Cleroux, P. Dashney, J. Laplerre, M. Foster

The main objective of the Animal Resources Group is to maintain animal facilities for the provision of high quality disease-free laboratory animals for use in biological research experiments carried out at NRC, especially in the Medical Biosciences and the Carbohydrate laboratories of the Division of Biological Sciences, and the Medical Sciences laboratory of the Division of Electrical Engineering. A limited number of rats and mice are provided to other non-NRC organizations.

The animal facility is comprised of two separate units. One unit houses germ-free, gnotobiotic, and specific pathogen free (SPF) rats, mice and rabbits, and the second houses all "conventional" animals procured from commercial breeding facilities in Canada and the U.S., minimizing the risk of contaminating the SPF unit.



Jagmohan Bhasin of Animal Resources, developing new techniques with Shelly Scott.

The rats used at NRC are physiologically and microbiologically defined and are free of human and rodent pathogens. These animals are primarily used as models to (a) understand the mechanism of normal and abnormal (cancer) cell proliferation, and (b) to study the molecular manifestations of certain disease states using magnetic resonance spectroscopy.

The athymic nude mice are mainly used as a host for the maintenance of tumour cell lines. Outbred strains of Swiss Webster mice and Balb/c are used for vaccination, challenge studies, and monoclonal antibody production.

Rabbits are mainly used for antisera production. The NRC SPF rabbit facility is now established and is in a position to provide very high quality, truly pathogen free rabbits for biomedical research. The Animal Resources facility is negotiating a possible transfer of this developed SPF rabbit production technology to major rabbit producing industries in Canada and/or the U.S.

The total number of animals produced and used depends mostly on the experimental program in the Division of Biological Sciences, and varies between 10,000 and 12,000 laboratory animals per year. The majority of animals used were rats, mice, pigs and rabbits. Presently, animals are supplied to a total of thirty-five scientists in the Division of Biological Sciences, five in Electrical Engineering, and five at the University of Ottawa.

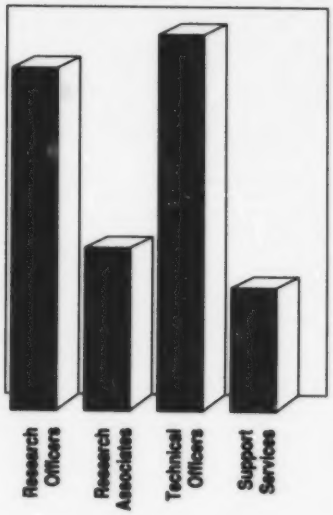
The Animal Resources Group also maintains a laboratory to provide microbiological and immunological services to the scientists in the Division of Biological Sciences, and some outside organizations including the Ministry of Agriculture, universities and practicing field veterinarians. The primary services provided to scientists in NRC include preparation of immune sera in laboratory animals, production of monoclonal antibodies, maintenance of tumor cell lines in rats and mice, euthanasia of laboratory animals, diagnosis, treatment and control of infections, diagnosis and prevention of zoonotic infections.

The Animal Resources Group also participates actively in collaborative research concerned with animal studies related to cancer, antigenic analysis of microorganisms, isolation of serotyping antigens, vaccination trials and immunity studies.

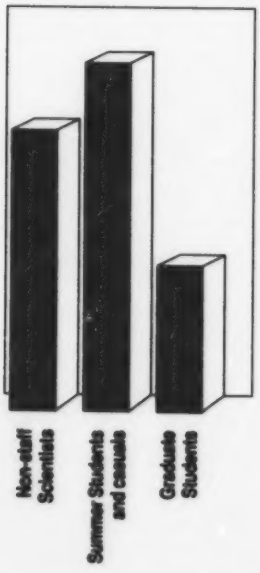
Administration and Services

Administrative Manager:
M. Dunlop
Office:
L.M. Boucher, A. Daley, C.J. Gobey, K.I. Hamelin, J.A. Legari, M. LePage, E. Monson, J.A. Strang
Technical Services:
J.P. Dumont, L. Langelier, J.S. Lynn, H.G. Lippke, Y.E. Leveille, P.W. McFadden
Electronic Design:
G. Charette, D.E. Harris, R.B. Holmes, W.P. Kasperek, R.J. Mausser, A. Ruppel, A. Simard, R.B. Toews
Supply:
P.J. Ashley, S.G. Belec, S.H. Fletcher, E.E. Grosser, T.C. Murphy
Photography:
T. Devecseri

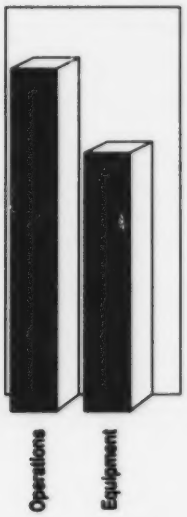
The NRC full-time staff target for the Division in 1989/90 was 178 people. In addition, there were many guest scientists and students collaborating and working in the laboratories. This is shown by the following distributions:



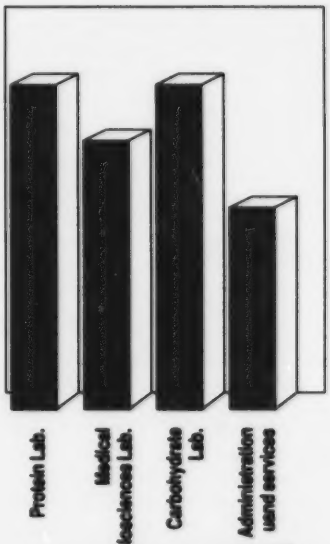
Margaret Dunlop



The NRC supplied budget in the 1989/90 fiscal year for the Division, other than for salaries, was:



The following graph provides the distribution of personnel over the laboratories and services:



The Divisional Office Staff
(Margaret Dunlop and Judi Strang)
(Chris Gobey, Lynda Boucher and Kathy Hamelin).

Directory of Staff

TITLE	NAME	DEGREES
Director's Office		
Director-General	I.C.P. Smith	BSc, MSc (Man.), PhD (Cambridge), FRSC, FilDr (HC. Stockholm)
Executive Assistant	A. Daley	
Director (Laboratories) Head (Carbohydrate Laboratory)	L. van den Berg	BSc, MSc (Wageningen), MSc (Man.)
Director (Industrial Affairs) Head (Medical Biosciences Laboratory)	G.H.M. Adams	BSc (McMaster), PhD (Carleton)
Secretary	M. Lepage	
Head (Protein Laboratory)	P.R. Carey	BSc, DPhil (Sussex)
Anaerobic Bioprocessing (Carbohydrate Laboratory)		
Senior Research Officers	A.W. Khan	BSc, MSc, PhD (Panjab), PhD (Manchester)
	H. Schneider	BSc (Sir George Williams), MSc (Western Ontario), PhD (McGill)
	I.V. Veliky	BSc (Slovak Polytech), PhD (Slovak Acad. Sci.)
	R.P. Overend	BSc, MSc (Salford), PhD (Dundee)
	K.G. Johnson	BSc, PhD (Alberta)
	A. Kudo	BSc, MSc (Kyoto), PhD (Texas)
	G.D. Sprott	BSc, MSc (Guelph), PhD (McGill)
	G.B. Patel	BSc (Sardar Patel), MSc, PhD (Sask.)
	K.J. Kennedy	BSc, MSc (Western Ontario), PhD (Ottawa)
Associate Research Officers	D.W. Armstrong	BSc, MSc (Ottawa), PhD (Carleton)
	R. Latta	BSc (Manitoba)
	W.D. Murray	BSc, MSc, PhD (Waterloo)
	S.J.B. Duff	BSc (Guelph), MESc (Western Ontario), PhD (McGill)
	F.W. Welsh	BSc (Manitoba), MSc, PhD (Cornell)
	E. Andras	BSc (Budapest), MSc (Ottawa)
Research Associates	N. Ross	BSc, PhD (McGill)
	C. Choquet	BSc, MSc (Laurentian), PhD (Ottawa)
Technical Officers	B.J. Agnew	BSc (Ottawa)
	K.M. Barber	BSc (Carleton)
	L.A. Brown	BSc (Guelph)
	C.J. Dicaire	Dipl (Algonquin)
	C.A. Elliott	BSc (Queen's)
	L.P. Fleming	BSc (Guelph)
	J.L. Labelle	
	K. Lamb	BSc (Guelph)
	K. Shaw	ONC (Belfast)
Animal Resources (Medical Biosciences Laboratory)		
Research Council Officer	J.L. Bhasin	BVSc, MVSc (Jabalpur), PhD (Davis)
Research Animal Care	M. Cleroux	
	J. Daoust	
	P. Dashney	
	M. Foster	
	J. Laperre	
	M. Levert	
Bioinformatics (Protein Laboratory)		
Senior Research Officers	R.L. Somorjai	BSc (McGill, PhD (Princeton)
	M. Zuker	BSc (McGill), PhD (M.I.T.)
Research Associate	S.Y. Le	BSc. (Shanghai U.), MS, PhD (Shanghai Inst.)
Computer Systems	L. Bramall	
	J. Ridgeway	

TITLE	NAME	DEGREES
Cellular Oncology (Medical Biosciences Laboratory)		
Principal Research Officer	J.F. Whitfield	BSc (McGill), MSc, PhD (Western Ontario)
Senior Research Officers	R.H. Rixon	BA, MA (U.B.C.), PhD (Western Ontario)
	J.P. MacManus	BSc (Ireland), PhD (Lancaster)
	P.R. Walker	BSc, PhD (Sheffield)
Associate Research Officers	J.P. Durkin	BSc, PhD (Waterloo)
	J.L. Schwartz	Certif. EG. Adv. Studies (Grenoble)
	M. Sikorska-Walker	BEng, PhD (Warsaw) MASc, PhD (Ottawa)
Research Associate	J. Kwast-Welfeld	MSc, PhD (Warsaw)
Technical Officers	M. Ball	BSc, MSc (Carleton)
	L. Dvarionas	
	R.J. Isaacs	Dipl (Algonquin)
	J.M. LeBlanc	BSc (Carleton)
	G.A.R. Mealing	BSc (Carleton)
	R.G. Tremblay	Dipl (Algonquin)
	T. Youdale	BSc (Ottawa)
Genetic Engineering of Proteins (Protein Laboratory)		
Principal Research Officer	S.A. Narang	BSc, MSc (Panjab), PhD (Calcutta), DSc hc (Carleton)
Associate Research Officer	J. Phipps	BSc, DEAE, PhD (Toulouse)
Research Associate	N.N. Anand	BSc (Panjab), MSc (Chandigarh), PhD (Cambridge)
Technical Officers	D. Bilous	BSc (Marianapolis)
	G. Dubuc	Dipl (Cdn. Soc. Lab. Tech.)
	J.J. Michniewicz	Dipl (Ryerson)
Immunochemistry (Carbohydrate Laboratory)		
Principal Research Officer	M.B. Perry	BSc, PhD, DSc (Bristol)
Senior Research Officers	H.J. Jennings	MSc, PhD (Queen's)
	D.R. Bundle	BSc (Nottingham), PhD (Newcastle)
	N.M. Young	BSc, PhD (Birmingham)
Associate Research Officers	C.R. MacKenzie	BSc (Acadia), MSc, PhD (Guelph)
	D.W. Griffith	BSc (Guelph)
	J.R. Brisson	BSc, MSc (Ottawa), PhD (Toronto)
	J.C. Richards	BSc, PhD (McMaster)
	E. Altman	BSc, MSc (Jerusalem), PhD (U.B.C.)
Research Associates	A.N. Anderson	BSc, PhD (Rhodes)
	L. Beynon	BA (Open), MSc, PhD (U.B.C.)
	K.R.P. Kartha	BSc, MSc (Kerala), PhD (Gujarat)
	J. Kihlberg	MSc, PhD (Lund)
	E. Kulakowska	MSc (Wroclaw), PhD (Polish Acad. Sci.)
	D. Leigh	BSc, MSc, PhD (Sheffield)
	B. Marsden	BSc, MSc, PhD (Birmingham)
	R. Oomen	BSc, PhD (Ottawa)
	W. Severn	BSc, PhD (Victoria)
	B.W. Sigurskjold	BSc (Copenhagen), MSc (Carlsberg), PhD (Denmark)
Technical Officers	F.P. Cooper	
	E. Eichler	MSc (Chem. Technol.)
	M.A.J. Gidney	BSc, MSc (Acadia)
	R.A.Z. Johnston	BSc, MSc (Manitoba)
	R.A. Leitch	BSc (Guelph), MSc (Ottawa)
	L. MacLean	Dipl (Ryerson)
	H. Seguin	
	B. Sinnott	

TITLE	NAME	DEGREES
Molecular Genetics (Protein Laboratory)		
Senior Research Officers	M. Yaguchi	B.Agric. (Tokyo), MS, PhD (California)
	B.F. Johnson	BSc (Penn. State), MA, PhD (U.C.L.A.)
	A. Nasim	BSc, MSc (Punjab), PhD (Edinburgh)
	V.L. Seligy	BSc, MSc, PhD (Toronto)
Research Council Officer	P.P. Matteau	BEng (Royal Military Coll.), MSc, PhD (Queen's)
Associate Research Officers	W.L. Sung	BSc, MSc (Oregon State), PhD (U.B.C.)
	M. Czuba	BSc, MSc (Toronto), PhD (Guelph)
Research Associates	I. Curran	BSc, MSc, PhD (Waterloo)
	M.A. Hefford	BSc (Carleton), PhD (Ottawa)
	A.P. Jahagirdar	MSc (Karnatok), MSc, PhD (Waterloo)
	G.K.E. Seifert	MSc (Lund)
	M. Ujiie	BSc (Niigata), PhD (Tsukuba)
Technical Officers	M. Dove	BSc, MSc (Carleton)
	P.H. Lanthier	Dipl (St. Lawrence)
	C.F. Rollin	Dipl (Hull Tech.)
	C. Roy	Dipl (Hull Tech.)
	E. Stephen	BSc (Halifax)
	T. Walker	Dipl (Algonquin)
	D.C. Watson	BSc (Brighton)
	D.M. Zahab	
Molecular Physiology (Medical Biosciences Laboratory)		
Senior Research Officers	R. Deslauriers	BSc (Laval), PhD (Ottawa)
	D.O. Foster	BSc, MSc (Western Ontario), PhD (Wisconsin)
	J.K. Saunders	BSc (Melbourne), PhD (McMaster)
	K.W. Butler	BSA (Toronto), PhD (Duke)
	H. Jarrell	BSc, MSc, PhD (Queen's)
Associate Research Officers	S. Ma	BSc, MSc (Hong Kong), PhD (U.B.C.)
	E. Preston	BSc, PhD (Alberta)
	H. Tang	BSc, PhD (Chinese Acad. Sci.)
	A. Ally	BSc (Western Ontario), MSc (Queen's), PhD (McGill)
Assistant Research Officers	K. Clarke	BSc (Flinders), PhD (Queensland)
	Y. Geoffrion	BSc, DSc (Laval)
Research Associates	R. Buist	BSc, PhD (McMaster)
	H. Xiong	MD (Shanghai)
Technical Officers	N. Haas	BSc (Ottawa)
	T. Kroft	CEGEP (Shawinigan)
	S. Lacelle	BSc (Ottawa)
	P. Mills	Dipl (Queen's)
	B. Nadeau	BSc, BA (Sir George Williams)
	L. Turner	
	T. Wessel	BSc (P.E.I.)
Protein Biochemistry and Spectroscopy (Protein Laboratory)		
Senior Research Officers	P.R. Carey	BSc, DPhil (Sussex)
	K.R. Lynn	BSc (Adelaide), PhD (Melbourne)
	A.G. Szabo	BSc (Queen's), MA, PhD (Toronto)
	G.E. Willick	BSc, MSc (U.B.C.), PhD (Illinois)
	R.E. Williams	BSc, PhD (Western Ontario)
Research Council Officer	S. Hasnain	BSc (Windsor), MSc, PhD (Ottawa)
Research Associates	K. Laderoute	BSc, MSc, PhD (Toronto)
	W. Neugebauer	MSc, PhD (Gdansk)
	M. Pozsgay	BSc, MSc (Debrecen), PhD (Hungarian Acad. Sci.)
	P. Tonge	BSc, PhD (Birmingham)
	K. Willis	BSc (Sheffield), PhD (Birmingham)
Technical Officer	J.R. Barbier	Dipl (Algonquin)
	R.G. Carriere	Dipl (Chem. Inst.)
	T. Hirama	BSc (Tokyo)
	D.T. Krajcarski	Dipl (Manitoba Inst. Technol.)
	T. Lessard	Dipl (Algonquin)
	L.R. Sans Cartier	BSc (Ottawa)

TITLE	NAME	DEGREES
Protein Crystallography (Protein Laboratory)		
Principal Research Officer	F.R. Ahmed	BSc (Alexandria), BSc, PhD (Leeds)
Senior Research Officers	G.I. Birnbaum	BS, AM, PhD (Columbia)
	C.P. Huber	BSc, MSc (Manitoba), DPhil (Oxford)
Associate Research Officer	D.R. Rose	BA (Penn. State), DPhil (Oxford)
Research Associates	R.L. Campbell	BSc (Queen's), PhD (Mass.)
	C.S. Kayden	HBSc (Lakehead), PhD (Victoria)
	X. Lee	BSc (Nankung), PhD (Grenoble)
Computer Systems	M.E. Pippy	
Technical Officer	R. To	BSc (National Taiwain U.)
Administration and Services		
Administrative Manager	M.V. Dunlop	BSc (W. Laurier)
Personnel (M-54)	C. Gobey	
Personnel (Sussex)	K. Harnetin	
Travel	L. Boucher	
Word Processing Services	J. Strang	
Electronic Design and Service		
Technical Officers	G. Charette	
	D. Harris	
	R. Holmes	
	W. Kasperski	
	R. Mausser	
	A. Simard	
	R. Toews	
Technical Services		
Technical Officers	J.P. Dumont	
	P.W. McFadden	
	Y. Leveille	
	H. Lippke	
	J. Lynn	
Laboratory Service Attendant	L. Langelier	
Photographer	T. Devecseri	Dipl (Algonquin)
Supply Services		
Supply Officer	E.E. Grosser	
Supply Clerks	S. Fletcher	
	P. Ashley	
	J. Legari	
	S. Belec	
	T. Murphy	

Research Facilities

- Fermentation facility ('C' level containment)– 0.5 L to 250 L fermentors. Tangential flow membrane harvest equipment as well as high capacity continuous flow centrifuges. Large volume 18 megohm water generation module.
- Pathogen containment and fermentation facility – 28 L and 75 L fermentors with cell harvesting equipment for culturing pathogenic organisms.
- Culture collection – in-house collection of more than 2500 species of bacteria, yeast and fungi, most of them available on request.
- Animal facility – specific pathogen free and gnotobiotic mice, rats and rabbits, nude mice, and conventional animals for research purposes.
- Nuclear magnetic resonance (NMR) – 600, 500, 360 (2), 200 MHz high resolution instruments; 300, 200 MHz broad line instrument; 200 MHz whole body spectrometer for spectroscopy and imaging.
- ESR – 9 GHz instrument.
- X-ray diffractometer with area detector.
- Raman spectroscopy – lasers and spectrographs for Raman spectroscopy in the visible and uv regions.
- Steady state and laser-based time resolved fluorescence instrumentation.
- Circular dichroism spectroscopy (uv and visible) – Jasco J600, thermostatted.
- Computers – Vax 11/750; high speed links to IBM mainframe and Vax 780 containing protein and DNA data bases and protein analysis routines.
- Molecular graphics system Evans and Sutherland, and Silicon Graphics (IRIS 4070 GT).
- Amino acid sequenator – (2) Applied Biosystem, gas phase; (2) Beckman 890, liquid phase.
- Amino acid analyzer – Durrum D500.
- Peptide synthesizer – BioSearch Sam II.
- DNA synthesizers – (2) BioSystems.
- C-level rDNA containment facility.
- Cation biofluorometer – Spex CM system – specificity for intracellular Ca^{2+}.
- Stereotaxic apparatus and microinjection capability.
- Cytofluorographic facility.
- Mammalian cell culturing laboratory.
- Hybridoma production laboratory.

Research Partnerships

The Division is involved in many collaborative research projects with industry, academic institutions and other government departments, and staff also participate extensively in outside activities, as indicated by the following lists:

Research collaborations with industry:

COMPANY	GROUP	DIVISIONAL STAFF
Alcan International Limited	Protein Biochemistry and Spectroscopy	R.E. Williams
Allelix Biopharmaceuticals	Cellular Oncology	J.F. Whitfield, R.H. Rixon
	Molecular Genetics	W.L. Sung
	Protein Biochemistry and Spectroscopy	G.E. Willick
	Protein Crystallography	D.R. Rose
Better Yield Insects	Anaerobic Bioprocessing	I. Veliky
Bruker Spectrospin Canada Ltd.	Molecular Physiology	J.K. Saunders, I.C.P. Smith
Canadian Bank Note Company	Protein Biochemistry and Spectroscopy	A.G. Szabo
Chembiomed Ltd.	Immunochemistry	D.R. Bundle
CIL Inc.	Protein Biochemistry and Spectroscopy	P.R. Carey, M. Poszgay
Cray Research Inc.	Biomolecular Modelling	M. Zuker
CSP Foods Limited	Anaerobic Bioprocessing	H. Schneider
Digital Equipment Corporation	Biomolecular Modelling	M. Zuker
F&C International	Anaerobic Bioprocessing	D.W. Armstrong
Forintek Canada Corp.	Protein Crystallography	G.I. Birnbaum D.R. Rose
	Molecular Genetics	M. Yaguchi
Gelda Scientific and Industrial Inc.	Molecular Genetics	M. Yaguchi
IAF BioChem International Inc.	Immunochemistry	H.J. Jennings
Labatts Brewing Company Limited	Molecular Genetics	V.L. Seligy
Long Life of Canada Limited	Molecular Genetics	M. Yaguchi
Paprican (Centres of Excellence)	Molecular Genetics	V.L. Seligy, M. Yaguchi
	Centre for Protein Structure and Design	P.R. Carey, D.R. Rose, G.E. Willick
Paques Lavalin	Anaerobic Bioprocessing	K.J. Kennedy, A. Kudo
Pegasus Biotechnology	Anaerobic Bioprocessing	D.W. Armstrong
Philom Bios	Anaerobic Bioprocessing	I. Veliky
Quesnel River Pulp Company	Anaerobic Bioprocessing	K.J. Kennedy, A. Kudo
Rhône-Poulenc	Molecular Physiology	J.K. Saunders
Safer Ltd.	Protein Biochemistry and Spectroscopy	P.R. Carey
Sepracor Inc.	Immunochemistry	D.R. Bundle

Research collaborations with industry: (continued)

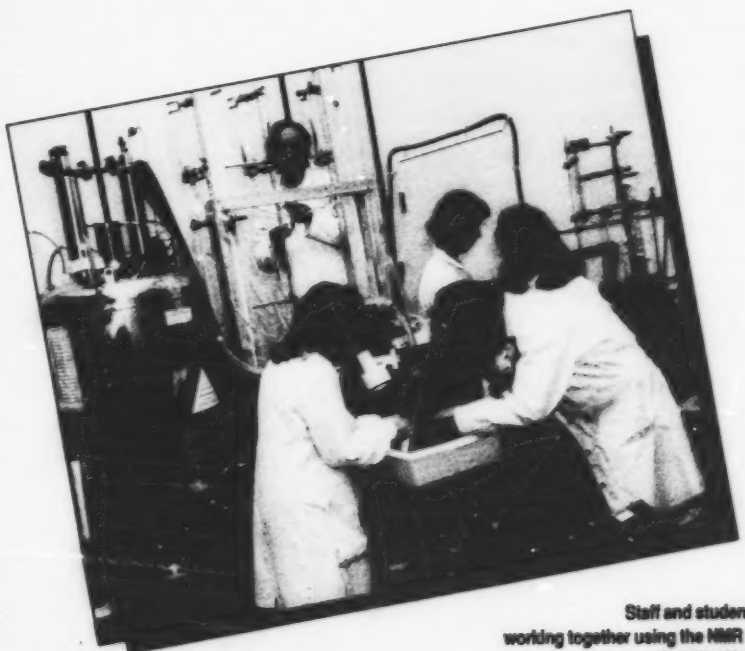
COMPANY	GROUP	DIVISIONAL STAFF
Siemens Medical Instruments	Molecular Physiology	I.C.P. Smith, J.K. Saunders
Varian Canada, Inc.	Protein Biochemistry and Spectroscopy	H.C. Jarrell
VETECH Laboratories Ltd.	Molecular Genetics	B.F. Johnson, V.L. Seligy
Veterinary Infectious Diseases Organization	Immunochemistry	E. Altman, D.R. Bundle, M.B. Perry
	Molecular Genetics	V.L. Seligy, M. Yaguchi
Diversified Research Laboratories, George Weston Group of Companies	Anaerobic Bioprocessing	G.B. Patel, G.D. Sprott

Research collaborations with academic institutions:

INSTITUTION	GROUP/ TOPIC	DIVISIONAL STAFF	NUMBER OF STUDENTS
Canadian Institute for Advanced Research	Biomolecular Modelling	M. Zuker	
Carleton University	Anaerobic Bioprocessing	D.W. Armstrong	2
	Genetic Engineering of Proteins	S.A. Narang	1
	Molecular Genetics	V.L. Seligy	10
	Molecular Physiology	J.K. Saunders, I.C.P. Smith	2
Carlsberg Institute, Denmark	Immunochemistry	D.R. Bundle	
Health Sciences Centre, Winnipeg	Molecular Physiology	J.K. Saunders I.C.P. Smith	
Institute of Nuclear Physics, Poland	Molecular Physiology	J.K. Saunders I.C.P. Smith	
Massachusetts Inst. of Technology	Protein Crystallography	D.R. Rose	
Networks of Centres of Excellence	Microbial Pathogens	M.B. Perry and others	
	Protein Engineering	P.R. Carey and others	
NIH-Brigham Women's Hospital	Immunochemistry	H.J. Jennings	
Ottawa Heart Institute	Molecular Physiology	R. Deslauriers	2
Queen's University	Cellular Oncology	J.F. Whitfield	
Scripps Institute, La Jolla, California	Cellular Oncology	R. Walker, M. Sikorska-Walker	
State University of New York	Biomolecular Modelling	M. Zuker	
University of Alberta	Cellular Oncology	J.P. MacManus	
University of British Columbia	Molecular Genetics	V.L. Seligy	
University of Frankfurt, Germany	Immunochemistry	J.-R. Brisson	

Research collaborations with academic institutions: (continued)

INSTITUTION	GROUP/ TOPIC	DIVISIONAL STAFF	NUMBER OF STUDENTS
University of Guelph	Anaerobic Bioprocessing	G.D. Sprott	
University of Manitoba	Molecular Physiology	I.C.P. Smith, J.K. Saunders	
	Immunochemistry	J.C. Richards	
University of Montreal	Immunochemistry	E. Altman	
University of Ottawa	Anaerobic Bioprocessing	K.J. Kennedy, G.D. Sprott	2
	Cellular Oncology	J.P. Durkin, J-L. Schwartz, J.F. Whitfield	2
	Molecular Genetics	V.L. Seligy	3
	Molecular Physiology	R. Deslauriers, K. Butler, I.C.P. Smith, J.K. Saunders, Y. Geoffrion	6 5
	Protein Biochemistry and Spectroscopy	P.R. Carey A.G. Szabo	4
University of Rochester	Biomolecular Modelling	M. Zuker	
Yale University	Protein Crystallography	G.I. Birnbaum	



Staff and students working together using the NMR at Building M-40

Research collaborations with other national and international government institutions:

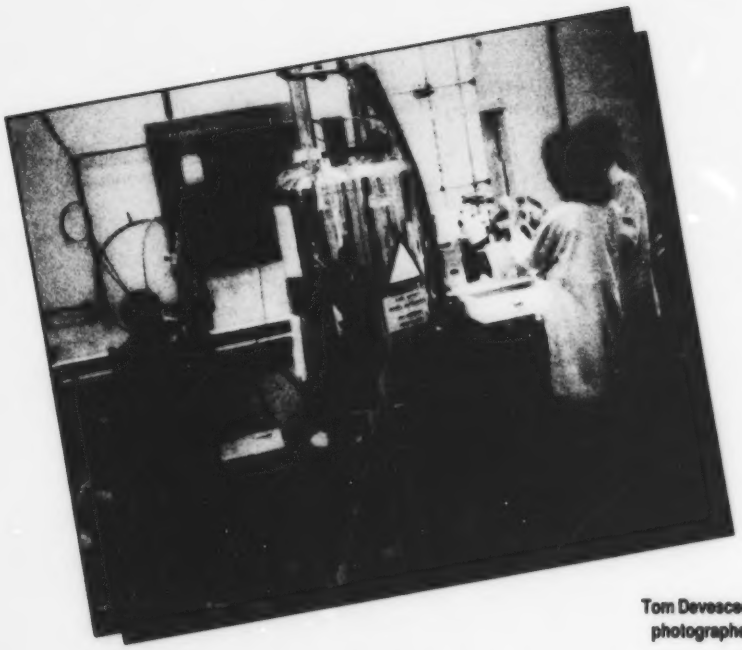
INSTITUTION	GROUP	DIVISIONAL STAFF
AECL	Molecular Physiology	R. Deslauriers, J.K. Saunders, R. Buist
Agriculture Canada	Immunochemistry Molecular Genetics Molecular Physiology Anaerobic Bioprocessing	J.C. Richards V.L. Seligy, M. Yaguchi D. Foster I. Veliky
CNRS, France	Immunochemistry Molecular Physiology Protein Biochemistry and Spectroscopy	M.B. Perry I.C.P. Smith H.C. Jarrell
Department of National Defence	Anaerobic Bioprocessing Immunochemistry	D.W. Armstrong D.R. Bundle
Forestry Canada	Molecular Genetics Protein Biochemistry and Spectroscopy	V.L. Seligy M. Pozsgay, P.R. Carey
Health & Welfare Canada	Anaerobic Bioprocessing Immunochemistry Molecular Physiology	D.W. Armstrong M.B. Perry, H.J. Jennings, N.M. Young E. Preston
IDRC/Technical University of Bombay India	Anaerobic Bioprocessing	K.J. Kennedy
INRA, France	Immunochemistry Cellular Oncology	D.R. Bundle, J.C. Richards J.P. Durkin, J.F. Whitfield
Institute National d'Optique	Molecular Physiology	J.K. Saunders
Institut Laue-Langevin	Protein Crystallography	X. Lee
Karolinska Institute, Sweden	Immunochemistry Molecular Physiology	D.R. Bundle, I.C.P. Smith
National Institute of Health, USA	Immunochemistry	H.J. Jennings
Shriners Hospital	Protein Biochemistry and Spectroscopy	S. Hasnain

Organizational activities outside NRC:

DIVISIONAL STAFF	ORGANIZATION / JOURNAL	ROLE
Bundle, D.R.	Chembiomed	Advisor
	American Chemical Society	Symposium Organizer
	Carbohydrate Research	Editorial Board
	Int'l Journal for Biological Macromolecules	Editorial Board
	Centre for Complex Carbohydrates, Athens, GA-	Scientific Advisory Board
Carey, P.R.	Int'l Conferences on Raman Spectroscopy	Advisory Committee
	Int'l Conferences on Interaction of Laser Light on Biological Objects	Advisory Committee
	Conference on Enzymes in Biotechnology	Advisory Committee
	European Conference on Spectroscopy in Biology	Advisory Committee
	Conference on Spectroscopy in Biology	Symposium Organizer
	Int'l Biophysics Satellite Meeting	Symposium Organizer
Deslauriers, R.	Int'l Society for Magnetic Resonance	Steering Committee
	External Ventricular Assist Device	Scientific Review Committee
	Canadian Journal of Spectroscopy	Associate Editor
	NMR in Biomedicine	Editorial Board
	Resonance	Editor
Foster, C.D.O.	Canadian Journal of Physiology and Pharmacology	Associate Editor
Jennings, H.J.	IAF Biochemicals	Advisor
	World Health Organization	Expert
	16th Int'l Congress of Chemotherapy	Symposium Organizer
Kennedy, K.J.	BIOQUAL Network	Secretary
	World Energy Congress	Committee Member
Narang, S.A.	International Centres of Genetic Engineering and Biotechnology	Panel of Scientific Advisors
	Methods in Molecular and Cellular Biology	Editorial Board
Nasim, A.	Academy of Third World Science	Fellow
Overend, R.P.	Energy, Mines & Resources	Scientific Authority
	Canadian Society for Peat and Peatlands	President
	Biomass, RERIC International Energy Journal	Editorial Board
	American Chemical Society	Symposium Organizer
	CANMET Energy Conversion 50/50 Contract Committee	Member
Patel, G.B.	Canadian Journal of Microbiology	Associate Editor
Schwartz, J.-L.	Spex Industries	Advisor
Seligy, V.L.	University of Toronto, Institute of Biotechnology	Advisory Board
	Int'l Committee Iridoviruses	Advisory Board
	MRC Fellowship Committee	Associate Chairman
	NSERC (CRD) Grants	Scientific Advisor
Smith, I.C.P.	Biophysical Society of Canada	President-Elect
	Canadian National Committee, Biophysics	Chairman
	Society for Magnetic Resonance in Medicine	Executive Committee
	Int'l Union of Pure and Applied Biophysics	Program Chairman, 10th Biophysics Congress
	Journal of Magnetic Resonance	Editorial Board
	Magnetic Resonance in Chemistry	Editorial Board
	Molecular Pharmacology	Editorial Board
	Molecular and Cellular Biochemistry	Editorial Board
Sprott, G.D.	Canadian Journal of Microbiology	Section Editor
Stephen, E.	Health and Welfare Canada	Secondment
van den Berg, L.	Energy, Mines & Resources	Member, Technical Advisory Board, Ethanol from Wood Program
Welsh, F.W.	Food Biotechnology Committee, Agriculture Canada	Member
Zuker, M.	Canadian Institute for Advanced Research	Fellow
	Computer Applications in the Biological Sciences	Associate Editor

University appointments for staff (Adjunct Professor):

DIVISIONAL STAFF	GROUP	UNIVERSITY
Ally, A.	Molecular Physiology	Ottawa
Armstrong, D.W.	Anaerobic Bioprocessing	Carleton
Carey, P.R.	Protein Biochemistry and Spectroscopy	Ottawa
Deslauriers, R.	Molecular Physiology	Ottawa
Durkin, J.P.	Cellular Oncology	Ottawa
Geoffrion, Y.	Molecular Physiology	Ottawa
Jennings, H.J.	Immunochemistry	Québec
Kennedy, K.J.	Anaerobic Bioprocessing	Ottawa
Narang, S.A.	Genetic Engineering of Proteins	Carleton, Ottawa
Nasim, A.	Molecular Genetics	Ottawa
Overend, R.P.	Anaerobic Bioprocessing	Sherbrooke
Perry, M.P.	Immunochemistry	Ottawa
Phipps, J.	Genetic Engineering of Proteins	Montréal
Saunders, J.K.	Molecular Physiology	Carleton, Sherbrooke
Schwartz, J.L.	Cellular Oncology	Montréal
Seligy, V.L.	Molecular Genetics	Carleton, Ottawa, Toronto
Smith, I.C.P.	Molecular Physiology	Ottawa, Carleton
Sprott, G.D.	Anaerobic Bioprocessing	Guelph, Ottawa
Sung, W.	Molecular Genetics	Ottawa
Szabo, A.G.	Protein Biochemistry and Spectroscopy	Ottawa
Whitfield, J.F.	Cellular Oncology	Ottawa
Young, N.M.	Immunochemistry	Ottawa



Tom Devescari,
photographer.